

## **REMARKS**

After entry of the present Amendment, claims 17-19 and 23-27 are pending in the application. Claim 17 has been amended to recite that a) and b) are "2 to 10." Support for the amendment can be found at least at page 7, 4<sup>th</sup> full paragraph and Table 1 at pages 10-16. Accordingly, no new matter has been introduced by way of the amendment.

The claims stand variously rejected. Each of the rejections is traversed as discussed below.

### **Abstract**

The examiner has requested that the Abstract point more clearly to the claimed subject matter. Applicants have included a replacement Abstract herewith.

### **Rejection under 35 U.S.C. § 112, second paragraph**

The Examiner has maintained the rejection claims 17-19 and 23-25 as indefinite for the recitation of "at least two" with regard to the length of the alkyl chain at a) and b). Applicants respectfully assert that the recitation of "at least two" is not *per se* indefinite, as the Examiner argues. However, to advance prosecution, Applicants have amended claim 17 to recite "2 to 10."

In view of the Amendment, Applicants request withdrawal of the rejection of claims 17-19 and 23-25 under 35 U.S.C § 112, second paragraph.

### **Rejection under 35 U.S.C. § 112, first paragraph**

The Examiner has maintained the rejection of claims 26 and 27 as not enabled. The Examiner argues that there is test data for "only two" exemplary compounds in the elected group and that the data shows "weak activation or no activation." The Examiner further argues that there is very little predictability in the art and as evidence, states that theophylline and caffeine have similar structures but differing properties. Finally, the Examiner states that "the state of the art is such that there are no drugs that can treat multi drug resistance or protein transfer." Applicants respectfully assert that the above reasoning is flawed and the conclusion of nonenablement is therefore unwarranted.

Addressing the Examiner's first argument that Applicants have provided data for "only two" compounds, Applicants respectfully remind the examiner that as originally filed, all compounds exemplified in the specification fell within the scope of the claims. The fact that a limited number of examples now fall within the scope of the claims is due to the restriction

requirement imposed by the Patent Office. It is manifestly unfair to limit Applicants' invention by way of restriction and then fail to consider Applicant's data showing efficacy of similar compounds as evidence of enablement. Moreover, it is well-settled that it is not necessary that a patent applicant test all the embodiments of his/her invention in order to meet the requirements of §112. *In re Angstadt*, 190 USPQ 214, 218 (CCPA 1976).

Further, the Examiner appears to have misconstrued Applicant's data. Table 3, to which the Examiner refers, includes both Accumulation Index data and Substrate Potential data for example compounds 6 and 15, both of which can be used in the method of rejected claims 26 and 27. The Accumulation Index, as taught in Reference Example 3, is a measure of a compound's ability to prevent extrusion of a fluorescent substrate by MDR1 in comparison to untreated cells. The Substrate Potential, as taught in Reference Example 4, is a measure of the ATPase activity of MDR1. If addition of the compound to isolated MDR1 expressing cell membranes results in weak or no activation of the ATPase activity, transport by MDR1 is inhibited. Thus, the Examiner's observation that the compounds exhibit "weak activation or no activation" weighs in favor of enablement. The Examiner is requested to note that there is no requirement that all of the compounds within a claimed genus exhibit the same degree of efficacy in order to meet the requirements of §112. *In re Gardner*, 177 USPQ 396 (CCPA 1973).

Addressing the Examiner's second argument regarding unpredictability in the art, Applicants acknowledge that slight differences in the structure of chemical compounds can result in differing biological properties. However, the "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate disclosed or known results to the claimed invention. MPEP 2164.03. With respect to the presently claimed invention, Applicants have shown in Example 85 that cells treated with compounds within the scope of the claims (and similar compounds having the same pyridine core structure but different substituents) effectively result in at least 5 times greater accumulation of fluorescence than control-treated cells. Moreover, many of the compounds result in no or weak activation of the ATPase function of the MDR1 protein, which as explained above, is an indirect measure of inhibition of transport by MDR1. Therefore, at least in view of Applicants' data, it is respectfully asserted that one of skill in the art would predict that the claimed methods would work.

As to the assertion that the prior art contains no compounds that have been shown to treat multidrug resistance, it appears that the Examiner questions the utility of the claimed methods. However, Applicants respectfully assert that the Examiner has not provided any evidence or factual support for such an assertion. Therefore, the Examiner has not met the

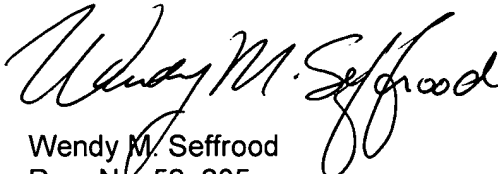
Patent Office's initial burden for challenging Applicants' presumptively correct assertion of utility. *In re Marzocchi*, 439 F.2d 220, 223 (CCPA 1971) ("Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence...")

Withdrawal of the rejection is respectfully requested.

### **CONCLUSION**

In view of the foregoing, reconsideration and allowance of claims 17-19 and 23-27 is respectfully requested. The Examiner is invited to contact the undersigned by telephone at the Examiner's convenience should any issues remain with respect to the Application.

Respectfully submitted,



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